

Hydrogen Bonding of Amide Groups in Dioxane Solution

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Lactams frequently have been used as model compounds to investigate amide to amide hydrogen bonding because the *cis* arrangement of C=O and N—H groups leads to dimerization exclusively and prevents complications arising from multiple equilibria between hydrogen-bonded chain polymers.¹⁻³ Various authors have employed infrared methods to investigate the dimerization of lactams in carbon tetrachloride, a solvent which is virtually inert from the standpoint of hydrogen bonding.¹⁻⁴ Relatively little work has been reported in solvents which are themselves capable of hydrogen-bond formation. Such studies lead to a net energy difference between initial and final states characterized by amide groups bonded to the solvent and to each other, respectively. The results are of

interest in assaying the role of hydrogen bonds in the secondary structure of proteins under conditions where amide–amide bonds can compete with amide–solvent bonds. The energy of interaction of even weak proton donors, such as chloroform, with an amide has been estimated at 2 kcal./mole.²

This communication reports a study of the dimerization of δ -valerolactam in a proton-accepting solvent, dioxane, by methods of infrared spectroscopy. One of the principal difficulties encountered in work with complex systems is proper evaluation of the temperature dependence of the absorption coefficients of various species.⁵ For the investigated system, a procedure involving some approximations is proposed which takes into account both solvent–solvent and solvent–solute interactions and which leads to internally consistent results over a wide range of temperature and concentration.

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 - (2) W. Klemperer, M. W. Cronyn, A. H. Maki, and G. C. Pimentel, *J. Am. Chem. Soc.*, **76**, 5846 (1954).
 - (3) R. C. Lord and T. J. Porro, *Z. Elektrochem.*, **64**, 672 (1960).
 - (4) H. E. Affsprung, S. D. Christian, and J. D. Worley, *Spectrochim. Acta*, **20**, 1415 (1964).
 - (5) G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman and Co., San Francisco, Calif., 1960, p. 77.

Experimental

δ -Valerolactam (Aldrich Chemical Co.⁶) was purified by distillation to remove traces of water. Dioxane (Fisher Certified Reagent) was refluxed with dilute hydrochloric acid for 12 hr., then refluxed over sodium for 24 hr. and distilled.⁷ Absorption spectra from 6000 to 7000 cm^{-1} were obtained with a Cary Model 14 instrument. Sample concentrations ranged from 0.1 to 0.8 mole/l. The absorption of each sample was investigated at 25, 45, and 65°. A water-jacketed controlled-temperature absorption cell of conventional design¹ and 25-mm. path length was employed.

Only one temperature-dependent absorption band of appreciable intensity, centering close to 6690 cm^{-1} ($\sim 1.495 \mu$), was observed in the investigated range. This band was assigned to the first overtone of the NH stretching mode of amide groups not involved in amide-amide H-bonding, on the basis of its temperature dependence and by comparison with spectra obtained in various other solvents (CCl_4 , CCl_3H) and the spectrum of the pure lactam. It should be pointed out that neither in dioxane solution nor in any other investigated solvent (or in the spectrum of the pure lactam) were bands of appreciable intensity found which could be assigned to overtones of NH stretching fundamentals of groups involved in amide-amide bonding. Although the corresponding fundamentals are very intense,¹⁻³ the overtones must be extremely weak. Figure 1A gives the observed peak absorbance of the investigated absorption band as a function of temperature and concentration, as observed in a 25-mm. cell.

Evaluation of Experimental Results

If no higher polymers are formed and if the solvent is inert, then the following relations hold

$$K'_x = \frac{C - M}{2M^2} \left(\frac{C + M}{2} + C_s \right) \quad (1)$$

$$M = A/\epsilon d \quad (2)$$

$$K'_x = \frac{C - A/\epsilon d}{2(A/\epsilon d)^2} \left(\frac{C + A/\epsilon d}{2} + C_s \right) \quad (3)$$

where K'_x is the dimerization constant in mole fraction units; C is the total solute concentration in moles per liter; C_s is the solvent concentration in moles per liter; M is monomer concentration in moles per liter; A is the absorbance of monomers; ϵ is the absorptivity or monomeric species; and d is the path length.

Rearrangement of (3) leads to

$$C_s/A = (\epsilon d/A^2)(C^2/2 + C_s C) - (4K'_x + 1)/2\epsilon d \quad (4)$$

The unknowns K'_x and ϵ can be obtained by setting

$$y = C_s/A \quad (4a)$$

$$x = (1/A^2)(C^2/2 + C_s C) \quad (4b)$$

and by plotting y vs. x . ϵd is given by the slope and K'_x is calculated from the intercept. The necessity to evaluate ϵ by extrapolation is eliminated.

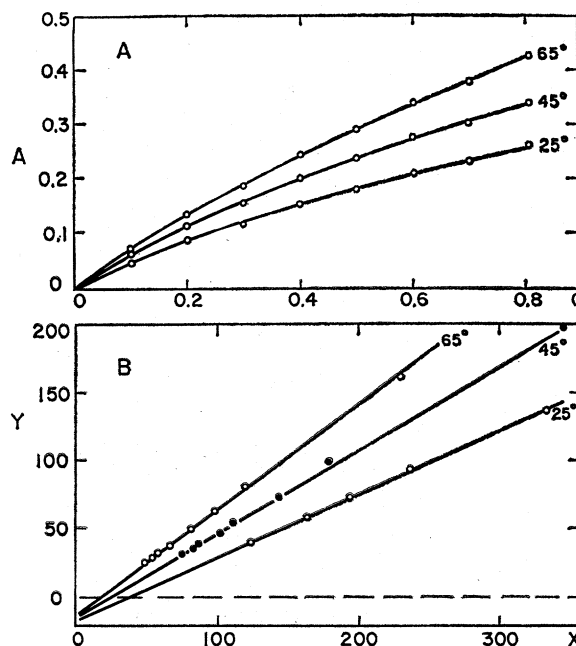


Figure 1. A: Observed absorbance of δ -valerolactam in dioxane solution at 1.495 μ ; path length: 25 mm. B: Graphical evaluation of absorptivity and dimerization constant; $y = C_s/A$; $x = (1/A^2)(C^2/2 + C_s C)$.

Figure 1B presents the results of the described graphical procedure. It is immediately obvious that the slope of the obtained lines varies with temperature, i.e., that the observed absorptivity [$\epsilon_{\text{obsd}} = (dA/dC)_{T, C \rightarrow 0}$] is strongly temperature dependent. An inspection of Figure 1A leads to the same conclusion.

If the monomer is heavily bonded to the solvent, then dimerization occurs by breaking up this complex and forming the dimer and two solvent molecules. In this case, eq. 1 holds for the dimerization of initially solvent-bonded monomers. Previous infrared studies have shown that amides are very strongly bonded to ethers,⁸ i.e., the monomer-solvent association constant

(6) Mention of specific firms and products does not imply endorsement by the U. S. Department of Agriculture over others of a similar nature not named.

(7) K. Hess and H. Frahm, *Ber.*, **71**, 2627 (1938).

(8) S. Mizushima, M. Tsuboi, T. Shimanouchi, and Y. Tsuda, *Spectrochim. Acta*, **7**, 100 (1955).

has a high value. If the association constant for solute-solvent interaction is much higher than the solvent-solvent association constant, eq. 3 is also applicable to the dimerization of initially solvent-bonded monomers, provided the temperature dependence of the apparent absorptivity is taken into consideration.

Figure 1B leads to the following numerical values: $T = 298^\circ\text{K.}$, $\epsilon_{\text{obsd}} = 0.184 \text{ l. mole}^{-1} \text{ cm.}^{-1}$, $K'_x = 4.1 \text{ (mole fraction)}^{-1}$; $T = 318^\circ$, $\epsilon_{\text{obsd}} = 0.246$, $K'_x = 4.2$; $T = 338^\circ$, $\epsilon_{\text{obsd}} = 0.295$, $K'_x = 4.0$.

The variation of K'_x is within experimental accuracy. Standard methods lead to: $\Delta H = 0 \pm 0.5 \text{ kcal./mole}$, $\Delta S^\circ = +3 \pm 0.5 \text{ e.u.}$ for the dimerization of initially solvent-bonded monomers. The entropy value refers to a standard state defined in mole fractions.

Discussion

The results suggest that the energy required to break amide-ether hydrogen bonds is approximately equal to the energy of formation of amide-amide bonds. The relatively high value of the association constant is thus a consequence of a positive standard entropy change upon dimerization. While the system is far too complex for a detailed discussion of entropy relations, a brief qualitative consideration might provide some insight. The "monomeric" system involves two

particles schematically represented by: $2 \times (\text{amide-dioxane})$. Upon dimerization, one *amide-amide* dimer (with two H bonds) and two free solvent molecules are formed, *i.e.*, the total number of particles is increased. At sufficiently high concentration, the positive value of ΔS° results in a considerable number of $\text{NH} \cdots \text{O}=\text{C}$ bonds being formed without a net change in enthalpy. The value of K'_x reported here is about 1/725 times the value given by Tsuboi¹ for dimerization of δ -valerolactam in carbon tetrachloride solution ($K_{\text{C}(\text{CCl}_4, 25^\circ)} = 280 \text{ moles/l.}$; $K_{\text{x}(\text{CCl}_4, 25^\circ)} = 2900 \text{ (mole fraction)}^{-1}$), reflecting the strong competition between dimerization and solvent interaction in the studied system.

The experimental data, as presented in Figure 1A, re-emphasize the necessity^{3,5} to determine the temperature dependence of apparent absorptivity values if thermodynamic quantities are deduced from absorbance measurements in complex systems. Our results also lend support to the conclusion⁹ that the anharmonicity of XH stretching fundamentals is reduced by hydrogen bonding.¹⁰

(9) See ref. 5, p. 114.

(10) The overtone frequency in dioxane solution is very close to the overtone frequency in CCl_4 solution. The fundamental frequency is substantially lower in dioxane solution.